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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/917,800	07/31/2001	Donna L. Mendrick	GENE-035/09US	1108

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COOLEY GODWARD KRONISH LLP
THE BROWN BUILDING - 875 15TH STREET, NW
SUITE 800
WASHINGTON, DC 20005-2221

EXAMINER	
MILLER, MARINA I	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/917,800	Applicant(s) MENDRICK ET AL.	
	Examiner Marina Miller	Art Unit 1631	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 13 October 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *13 October 2006*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *92-129*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

MARJORIE A. MORAN
PRIMARY EXAMINER
Marjorie A. Moran
10/30/06

Continuation of 3. NOTE: filed amendments raise a new issue under 35 USC 112, first paragraph, enablement and written description, and 112, second paragraph, e.g., the limitation "wherein said at least ten genes are selected from the genes AND ESTs [[sequences listed]]."The proposed amendments also raise an issue of new matter. Applicants pointed to p. 43 of the specification and page 48, paragraph [0196] (note: the originally filed specification does not contain numbered paragraphs) for support of the newly filed limitation. However, the originally filed specification, drawings, and claims do not support the new limitation.

Continuation of 11. does NOT place the application in condition for allowance because: As the amendment is not entered, applicants' arguments with regard to the proposed claims are not persuasive.

With regard to the arguments NOT directed to the proposed amendments.
Claims 92-129 were previously rejected for lack of enablement because (1) a database comprises data from blood, liver, kidney, etc., and therefore one cannot predict hepatotoxicity by comparing data from liver to the database; (2) the specification does not disclose whether the comparison in Tables 3A-3S is performed between expression profiles in liver, kidney, brain, blood, etc.; (3) not all genes of Table 1 are implicated in LIVER toxicity; and (4) it is not disclosed whether comparison recited in claims 105 and 124 is performed with normal liver tissue or diseased tissue.
Applicants argue with respect to issue (1) that the disclosed database may be used to identify expression levels in liver tissue and pointed to various pages in the specification. In response, it is noted that the specification discloses that various tissues are collected (blood, liver, heart, kidney, etc., p. 37-39) for generating Tables 3A-3S. Also, a review of the Tables shows that various "genes" are isolated from a spleen library (A924307, GLGC ID 3972) and lung library (AA818741, GLGC ID 4292). Thus, one skill in the art would not know how to predict LIVER toxicity without undue experimentation. Further, applicants argue that the specification discloses that the Tables may be used for detecting hepatotoxicity after the exposure to known hepaptotoxins. However, as the Tables comprise various tissue, the specification does not disclose that known hepatotoxins ONLY affect liver and do not affect other cells. Also, Tables 3A-3S do not comprise expression LEVELS, but only expression information, and therefore "comparing" expression levels to the expression information in the Tables requires further processing of the test expression levels. In addition, the specification does not provide guidance how to compare gene expression levels with mean values. LOD scores, etc. of Tables 3A-3S.
With regard to issue (2)-(3), applicants argue that all genes presented in Tables 3A-3S are expressed in liver tissues. However, as it is noted above, various "genes" are isolated from a spleen library (A924307, GLGC ID 3972) and lung library (AA818741, GLGC ID 4292). It is not readily apparent that those genes are also expressed in liver and involved in hepatotoxicity, although those genes might be involved in other toxicities. Moreover, as set forth in the previous office action, it is not clear whether, for example, GLGC ID 4097-4168 and 11426 to 11504 are implicated in liver toxicity because their pathways are not known. Also, 1 kp mRNA sequence (AA924307, GLGC ID 3972) represents a sequence of unknown location and function, and therefore is in not apparent that this "gene" is involved in liver toxicity.
With respect to issue (4), applicants argue that one skill in the art would recognize that claims 92 and 111 recite normal liver tissue before and after exposure to a known hepatotoxin. In response, it is noted that Table 3D comprises data directed to necrosis with and without fatty liver wherein the specification does not disclose that the comparison is made for normal and diseased liver tissue, as set forth in the previous office action. Thus, for the reasons set forth above and in the previous office actions, the enablement rejection is maintained.

With regard to the art rejection of claims 92, 106, and 111 under 35 USC 102(b) over Farr, US 5,811,231, applicants argue that Farr does not disclose ten genes from any ONE of Tables 3A-3S. It is noted, that Farr discloses a plurality of genes expression profiles (Tables 1-2 and claims 9-15) including those disclosed in Tables 1-3 and measuring effect of a chemical stress on HepG2 cells (col. 5-6; claims 9-15, tables 1-2), as set forth in the previous office actions. Instant Tables 1 comprises thousand of genes identified by GLGC ID numbers. Tables 3A-3S comprise expression information corresponding to "genes" identified in randomly by GLGC ID. It is unduly burdensome to search Tables 3A-3S in order to determine which gene from Table 1 is included in which of Tables 3A-3S. After a reasonable search, the examiner concludes that a variation of ten genes disclosed by Farr can be found in any one of Tables 3A-3S. Therefore, the examiner maintains that Farr anticipates claims 92, 106, and 111, and the rejection is also maintained.

With regard to the rejection of claims 92, 97-101, 111, and 116-120 under 35 USC 103(a) over Farr, US 5,811,231, applicants argue that Farr does not disclose ten genes from any ONE of Tables 3A-3S. The answer to the arguments is set forth above. Therefore, the examiner maintains that Farr makes obvious claims 92, 97-101, 11, and 116-120, and the rejection is also maintained.

With regard to the rejection of claims 92, 97-101, 11, and 126 under 35 USC 103(a) over Farr, US 5,811,231, in view of Lashkari et al., PNAS, 94:13057-13062 (1997), applicants argue that neither Farr not Lashkari discloses ten genes from any ONE of Tables 3A-3S. The answer to the arguments is set forth above. Therefore, the examiner maintains that Farr and Lashkari make obvious the instant claims, and the rejction is also maintained.